

2019 Multiscale Modeling Consortium Meeting - Translation and Dissemination (March 6-7, 2019)

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Title of Grant: Microconnectomics of neocortex: a multiscale computer model

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Abstract: We have explored the relation of structure to dynamics of brain primary motor cortex (M1) circuits -- crucial for fine motor control -- using a detailed computational model of M1 circuits. We use the model to explore various candidates for the neural codes underlying movement. Our M1 model includes over 10,000 neurons distributed across the cortical layers. Corticospinal cell models accurately reproduce the electrophysiology and morphology of real neurons. ~30 million synaptic connections reproduce cell type- and location connectivity patterns obtained from experimental studies. It also simulates inputs from the main cortical and thalamic brain regions that project to M1.

The Granger causal dynamics of the circuitry reflected the canonical model of activation from Layer 4 (L4) to L2/3 to L5 with frequency bands of greatest transfer generally in the high beta (20-30 Hz) and low gamma (30-40 Hz) range. Inputs from motor-related vs. sensory related regions created different output activation patterns in the PT (pyramidal tract) major output pathway. Two PT output patterns could be identified, corresponding to upper L5B and lower L5B. Modulation of HCN channels in corticospinal neurons also served as a switch to regulate output, a potential mechanism to convert motor planning into motor execution.

1. **Context:** Data obtained primarily from brain slice work was used to cross over to explain dynamics of in vivo brain area M1.
2. **Data:** We attempted as far as possible to utilize coherent data, basing many parameters on data obtained from a single species (mouse), a single strain, a restricted age range and from one laboratory. However, these data were necessarily incomplete, and we have therefore had to combine additional data from multiple other sources.
3. **Evaluation:** We compare model activity to in vivo experimental measures at two main scales: single neuron firing patterns; local field potentials (LFPs).
4. **Limitations:** Limited parameter data is available as noted above. We are simulating a small piece of cortex in isolation. We are typically stimulating with white noise inputs although we also have access to some periods of measured input trains. There is no point-to-point cortical wiring information available; only population to population and area to area average projection densities.
5. **Version control:** Mercurial.
6. **Documentation:** Simulations designed in a partially self-documenting high-level declarative wrapper (NetPyNE). Additional comments are provided for each declarative section.
7. **Dissemination:** Full model will be shared on ModelDB and Open Source Brain after publication (ModelDB only accepts published models). Description of current version of model is available on biorxiv.
8. **Independent reviews:** Porting to NEST (see below) involves review of our assumptions and comparison with existing NEST cortical model. Simplified version of model is being used as a teaching tool.
9. **Test competing implementations:** Model is being ported to the NEST simulator. NEST offers a different approach with different level of multiscale detail so results of this implementation will be particularly interesting. Port to HPC is complete. With upload to NeuroML, model can be downloaded to run with other simulators. Model is being recreated using a related graphical interface by MetaCell corporation.
10. **Conform to standards:** Broad standards being utilized include ModelDB, SONATA, NeuroML.